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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,976	09/20/2000	Lawrence W. Stanton	SCIOS.014A	8472

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EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	#12

DATE MAILED: 04/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/665,976	Stanton et al
Examiner	**Art Unit**
Jehanne Souaya	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 22, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5,7*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Please note that the art unit designation for the examiner has changed from 1655 to 1634.

Election/Restriction

Applicant's election of Group I, claims 1a-g, 2-7 with traverse is acknowledged. Claim 1 has been amended to delete the subject matter in section (I). Claims 8-29 have been canceled. An action on the merits of amended claim 1 and claims 2-7 follows.

Priority

Applicant's claim for priority to provisional application 60/156,280 filed 9/27/1999 is acknowledged. The claims have been awarded the benefit of the earlier filing date as the subject matter in the claims was present in the provisional application.

Claim Objections

1. Claim 6 is objected to because of the following informalities: the recitation of the phrase "nucleic acid" lacks the article "a". This can be easily overcome by reciting instead "a nucleic acid" Appropriate correction is required.

Claim Rejections - 35 USC § 112

Indefinite

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 1, in sections a, b, e, and f, is indefinite over the phrase "at least about" because the metes and bounds of the invention are not clear. As the CAFC noted, and affirmed, regarding the district court determination of this phrase in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. (CA FC) 18 USPQ2d 1016 at page 1031 "the court held the "at least about" claims to be invalid for indefiniteness."

B) Claim 1, in section c, is indefinite in the recitation of "or inactivated variant" as it is unclear if the "the inactivated variant" refers to a polypeptide where the transmembrane domain is inactivated or whether any portion of the polypeptide could be inactivated.

C) Claim 1, in section d is indefinite in the recitation of "stringent conditions" as this language encompasses different reaction conditions such that the degree of complementarity needed to achieve hybridization between the nucleic acid sequence claimed and SEQ ID NO 2 is unclear. Stringent conditions can encompass conditions of "low stringency", "moderate

stringency", and "high stringency". The claim does not make clear what conditions are encompassed by the language and therefore the metes and bounds of the claim are unclear.

D) Claim 1 in section d is indefinite in the recitation of "coding region of SEQ ID NO: 2" because it cannot be determined if this phrase refers to the region that codes for the polypeptide of SEQ ID NO 1 or if it refers to the whole length of SEQ ID NO 2, which in figure 2 is shown to code for a number of amino acids on either side of the polypeptide of SEQ ID NO 1.

E) Claim 5 is indefinite in the recitation of the term "capable" as it is unclear if the claimed product actually exhibits the function of expressing a poly or oligonucleotide of claim 1 or whether the claim encompasses that it "could" exhibit this function but does not.

Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide comprising SEQ ID NO 1, an isolated nucleic acid molecule encoding amino acids 25 to 236 of SEQ ID NO 1, an isolated nucleic acid molecule comprising the sequence of SEQ ID NO 2, the complement thereof, and a vector or host cell comprising such, does not reasonably provide enablement for a nucleic acid molecule

comprising: a polynucleotide encoding a polypeptide having at least about 80% sequence identity with amino acids 25-236 of SEQ ID NO 1, a polynucleotide encoding a polypeptide having at least about 80% sequence identity with amino acids 25 to 214 of SEQ ID NO 1, a transmembrane domain deleted or inactivated variant of a polynucleotide encoding amino acids 25 to 236 of SEQ ID NO 1, a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO 2 and encoding a polypeptide having at least one biological activity of the polypeptide encoded by SEQ ID NO 2, a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25-214 of SEQ ID NO 1 wherein the polynucleotide encodes a polypeptide having at least one biological activity of the polypeptide encoded by SEQ ID NO 2, a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25-236 of SEQ ID NO 1 wherein the polynucleotide encodes a polypeptide having at least one biological activity of SEQ ID NO 1, complements thereof, a polynucleotide encoding a polypeptide comprising amino acids 25 to 214 of SEQ ID NO: 1, or vectors and host cells comprising such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims as written broadly encompass mutants, variants, and homologs of SEQ ID NOS 1 and 2 from any source. The specification teaches the polypeptide of SEQ ID NO 1 and the polynucleotide of SEQ ID NO 2. The specification teaches that using micro array analysis, the expression level of the gene corresponding to clone P00188_D12 (SEQ ID NO 2) was about

2 fold down regulated in a myocardial infarction rat model, 2.5 fold down regulated in a cardiac hypertrophy rat model, and about 2 fold up regulated in a viral myocarditis mouse model (p. 65). The specification teaches that the deduced amino acid sequence was determined (SEQ ID NO 1) and the open reading frame "contains 236 amino acid residues, of which approximately the first 24 residues show characteristics of a putative signal sequence and a probable membrane spanning region at positions 215-235".

Polynucleotides encompassed by the claims, such as: a polynucleotide encoding a polypeptide having 80% sequence identity with amino acids 25 to 214 or 236 of SEQ ID NO:1, a transmembrane domain deleted or inactivated variant of the polynucleotide encoding amino acids 25 to 236 of SEQ ID NO 1, or to a polynucleotide that hybridizes under stringent conditions with the complement of the coding region of SEQ ID NO 2, or polynucleotides that encode at least 50 contiguous amino acids from amino acids 25 to 214 or 236 of SEQ ID NO 1, or complements thereof; include mutants, variants, and homologs of SEQ ID NOS 1 and 2, resulting from missense, frameshift and truncation mutations, from any source, which have not been taught in either the specification or the art. The recitation of "which encode at least one biological activity of the polypeptide encoded by SEQ ID NO 2" does not further limit claim 1 in sections d-f because neither the specification nor the claim make clear what biological activity is encompassed by the claim. The biological activity could be the ability to bind to an antibody, or to fold into a stable conformation, which is not specific to the biological activity or function of the polypeptide of SEQ ID NO 1. It is also noted that the specification does not teach the

specific biological activity or function of the polypeptide of SEQ ID NO 1. With regard to claim 2, at page 38, the specification teaches that amino acids 215 to 235 "have been tentatively identified as membrane spanning segments". The specification teaches that the present invention includes amino acid sequence variants of the native rat polypeptide of SEQ ID NO 1, or its analogs *in any other animal*, and include sequences with more than one amino acid substitutions, or polypeptides in which the membrane spanning region or regions are deleted or inactivated. Therefore, the specification teaches that the recitation encompassed by "a polynucleotide encoding a polypeptide comprising amino acids 25 to 214 of SEQ ID NO 1" includes sequences with more than one amino acid substitutions, or polypeptides in which the membrane spanning region or regions are deleted or inactivated. With regard to claim 1, section d, the claim is confusing in the recitation of "coding region of SEQ ID NO: 2" because it cannot be determined if this phrase refers to the region that codes for the polypeptide of SEQ ID NO 1 or if it refers to the whole length of SEQ ID NO 2, which in figure 2 is shown to code for a number of amino acids on either side of the polypeptide of SEQ ID NO 1.

The specification, however, does not teach the function of the polypeptide of SEQ ID NO 1, nor how the biological activity or expression of this polypeptide is associated with any of the animal models taught in the specification. The specification has not demonstrated which amino acids or domains of the polypeptide of SEQ ID NO 1 are necessary for the activity of the polypeptide. The specification has not taught the function of the amino acids that are "coded" by SEQ ID NO 2, on either side of SEQ ID NO 1, as shown in figure 2 of the specification. The

specification has not taught any biological assays that the skilled artisan could use to determine amino acids or domains of the polypeptide of SEQ ID NO 1 that are responsible or necessary for its biological activity. While the specification teaches at page 38, that amino acids 215 to 235 "have been tentatively identified as membrane spanning segments", the specification has not taught that this "tentative" transmembrane domain is essential for the activity of the polypeptide of SEQ ID NO 1, and if it is, the specification has not taught which amino acid mutations (ie: substitutions, deletions or insertions) would lead to an "inactivated" transmembrane domain or an "inactivated" protein. Neither the specification nor the art teach the specific biological activity of the polypeptide encoded by SEQ ID NO 2, so that the skilled artisan might be able to predict which changes would result in polypeptides with either retained or altered biological activity. It is known for nucleic acids as well as proteins that even a single nucleotide or amino acid change or mutation can destroy or alter the function of a biomolecule in many instances, albeit not in all cases (see Proudfoot et al, Journal of Biological Chemistry, vol. 271, pp 2599-2603, which teaches that extension of recombinant human RANTES by a single residue [Met-RANTES] at the amino terminus was sufficient to produce a potent and selective antagonist - see abstract). The effect of these changes are largely unpredictable as to which ones have a significant effect verses not.

A correlation between mutants, variant and homologs encompassed by the claims and a specific biological activity is clearly unpredictable in light of the lack of guidance from the specification and the state of the art with regard to the specific biological function or activity of

the polypeptide encoded by SEQ ID NO: 2. Since neither the specification nor the art teach the specific biological function or activity of the polypeptide of SEQ ID NO 1, nor how the skilled artisan could modify the polypeptide of SEQ ID NO 1 to obtain a polypeptide with either retained or modified activity, the skilled artisan would be required to perform undue experimentation to make or use the polynucleotides that encode biologically active or altered polypeptides encompassed by the broadly claimed invention. To practice the invention as broadly as it is claimed, the skilled artisan would first have to determine the function or specific biological activity of the polypeptide of SEQ ID NO 1. The skilled artisan would then have to develop an assay by which to measure biological activity and would have to determine what amino acid residues were important for such specific activity, and then would have to determine which amino acids could be modified to either retain biological activity or to result in a protein with altered activity. Given that the art teaches that a single amino acid change can alter the function of a biomolecule and that some of these changes are unpredictable, and given that the specification does not a) teach the function of the polypeptide of SEQ ID NO 1, and b) provide any guidance as to an assay that the skilled artisan could use to measure the biological activity of the claimed polypeptide, such analyses would require trial and error, thus constituting undue experimentation. It is noted that because the skilled artisan would be required to perform undue experimentation to make and use the polynucleotides of claims 1 and 2, undue experimentation would also be required to make or use the complements of these nucleic acids and vectors or host cells comprising these polynucleotides.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al (US Patent 5,719,125, 2/17/1998).

It is noted that the term "coding region" in section d of claim 1 is being interpreted to mean the entire sequence of SEQ ID NO 2, as it is unclear if the claim encompasses the region that codes for the polypeptide of SEQ ID NO 1 or if it refers to the whole length of SEQ ID NO 2, which in figure 2 is shown to code for a number of amino acids on either side of the polypeptide of SEQ ID NO 1. Suzuki teaches the sequence of SEQ ID NO 11, a 60 mer, the complement of which contains 34 contiguous nucleotides that are identical (positions 12-45 of SEQ ID NO 11) to SEQ ID NO 2 from positions 841 to 874. Thus the sequence taught by Suzuki is the complement (refers to section g of claim 1) of a sequence which can hybridize to the complement of the "coding region" of SEQ ID NO 2. Thus, as section d of claim 1 does not recite the level of stringency of the hybridization conditions, and the claim does not recite what biological activity of the polypeptide encoded by SEQ ID NO 2 that the claim refers to (for example, the one biological activity of the polypeptide could be it's ability to bind to an antibody,

or to fold into a stable conformation), claim 1, section g has been interpreted broadly to encompass SEQ ID NO 11 taught by Suzuki.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession number AA891470 (June 16, 1998).

It is noted that the term "coding region" in section d of claim 1 is being interpreted to mean the entire sequence of SEQ ID NO 2, as it is unclear if the claim encompasses the region that codes for the polypeptide of SEQ ID NO 1 or if it refers to the whole length of SEQ ID NO 2, which in figure 2 is shown to code for a number of amino acids on either side of the polypeptide of SEQ ID NO 1. AA891470 corresponds to a nucleic acid sequence of 459 nucleotides, the complement of which, from position 1 to position 446 is almost identical (only contains 3 mismatches) to nucleotides 395 to 840 of SEQ ID NO 2. Thus the sequence of AA891470 is the complement (refers to section g of claim 1) of a sequence which can hybridize to the complement of the "coding region" of SEQ ID NO 2. Thus, as section d of claim 1 does not recite the level of stringency of the hybridization conditions, and the claim does not recite what biological activity of the polypeptide encoded by SEQ ID NO 2 that the claim refers to (for example, the one biological activity of the polypeptide could be it's ability to bind to an antibody, or to fold into a stable conformation), claim 1, section g has been interpreted broadly to encompass the sequence of AA891470. Further, sections e and f are drawn to a polynucleotide encoding at least about 50 contiguous amino acids from amino acids 25 to 214 and 25-236 of

SEQ ID NO 2. The complement of the nucleic acid of AA891470 encodes amino acids 157 to 224 (67 amino acids) of SEQ ID NO 2 (positions 131-331 of AA891470). Because sections e and f of claim 1 do not recite what biological activity of the polypeptide encoded by SEQ ID NO 2 that the claim refers to, claim 1, section g has been interpreted broadly to encompass the sequence of AA891470.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-6 of copending Application No. 09/809545. Although the conflicting claims are not identical, they are not patentably distinct from each other. For example, claim 1, section c of the '545 application recites "a polynucleotide encoding amino acids 1 to 236 of SEQ ID NO 6" which is encompassed by the following recitations in claims from the '976 application (it is noted that SEQ ID NO 6

from the '545 application is identical to SEQ ID NO 1 from the '976 application): Claim 1, section a of '976 recites a nucleic acid molecule comprising a polynucleotide encoding a polypeptide having at least about 80% sequence identity with amino acids 25 to 236 of SEQ ID NO 1, claim 1 section d of '976 recites a polynucleotide hybridizing under stringent conditions with the complement of the coding region of SEQ ID NO 2, claim 2 of '976 recites a polynucleotide encoding a polypeptide *comprising* amino acids 25 to 214 of SEQ ID NO 1, claim 3 of '976 recites a polynucleotide encoding a polypeptide comprising amino acids 25 to 236 of SEQ ID NO 1. Claim 3 of '545 and claim 4 of '976 are coextensive in scope as claim 3 of '545 is drawn to, in the alternative, a polynucleotide dependent on claim 1 that comprises a sequence of SEQ ID NO: 5, while claim 4 of '976 is drawn to a polynucleotide dependent on claim 1 that comprises a sequence of SEQ ID NO 2, where SEQ ID NO 5 from '545 is identical to SEQ ID NO: 2 from '976. Claims 5-7 from the '976 application and claims 4-6 from the '545 application are dependent respectively on claim 1 from each application, and are drawn to vectors and host cells and are thus also coextensive in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. No claims are allowable. SEQ ID NOS 1 and 2 are free of the prior art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
4/10/02